2. Non-technical Abstract

Lung cancer is the most lethal malignancy in the United States, claiming over 150,000 lives each year and with an overall 5-year survival of 12 – 14%. New treatments are needed. One possible approach is the use of antigen-specific cancer vaccines. It is hoped that such vaccines can trigger the patient's own immune system to attack the cancer. Cancer antigens are typically proteins which are expressed at high levels in cancer cells, but are expressed at low levels or not at all in non-cancerous cells. Cancer-testis (CT) antigens are one of several categories of tumor antigens. These antigens are normally expressed only in germ cells in the testis and in various types of cancers. NY-ESO-1 is the most immunogenic CT antigen known to date. Cancer patients with NY-ESO-1 positive tumors have been show to generate spontaneous immune responses to NY-ESO-1.

Clinical trials have been performed with NY-ESO-1 vaccine used as either protein or peptides, which are parts of proteins, or DNA in viral vectors. In the latter form, the genetic material from a weakened virus is modified so that infected cells will make the NY-ESO-1 protein. In these trials, the NY-ESO-1 antigen has demonstrated specific immune responses following vaccination.

In this proposed phase I trial, we plan to immunize eligible lung cancer patients with NY-ESO-1 plasmid DNA vaccine, delivered by PowderJect® device. Plasmid DNA is a small circle of DNA that can be grown in bacteria. When purified and delivered to human cells, it triggers production of a protein, such as NY-ESO-1, but no new copies of the plasmid DNA are made. PowderJect® is a helium-powered, particle-mediated epidermal delivery (PMED) system designed to deliver protein or DNA vaccines intraepidermally. With this system, microscopic dry powders are delivered into the skin through tiny holes. These holes are too small and shallow to cause pain or bleeding. This delivery method has been shown to successfully induce antibody and T cell responses against hepatitis B antigen in humans.

PowderJect® has formulated a NY-ESO-1/PMED vaccine, consisting of plasmid (pPJV7611) containing NY-ESO-1 DNA coated onto microscopic gold particles. This formulation is expected to deliver NY-ESO-1 plasmid DNA to specialized cells. Some of these cells are professional antigen presenting cells (APCs). These cells, called Langerhans cells, are located in the outermost layer of the skin, the epidermis, and function to take up antigens. The APCs containing the plasmid DNA will make some amount of full-length NY-ESO-1 protein. They will also process some NY-ESO-1 protein to smaller peptides. These peptides are used to activate T cells which are an important part of the immune response. Some of the T cells (called $CD8^+$ cells) will see the same NY-ESO-1 peptides on the surface of lung cancer cells which will trigger them to kill the cancer. Other T cells (called $CD4^+$ cells) will see other NY-ESO-1 peptides on phagocytic cells near the cancer. These cells then make growth factors which help the $CD8^+$ cells to kill the cancer and which help B cells make antibodies to full-length NY-ESO-1 protein. These antibodies can also contribute to cancer cell death. It is hoped that NY-ESO-1 DNA delivered by PowderJect® PMED will lead to humoral and cell-mediated immune responses that are potentially stronger than those induced with other antigen forms and delivery methods.

The objectives of the study are:

- To evaluate the safety of the NY-ESO-1 plasmid DNA (pPJV7611) cancer vaccine.

- To monitor the immune response to NY-ESO-1 when administered as PMED. Humoral responses will be measured by detecting NY-ESO-1 serum antibody by ELISA. Cellular immune response will be measured in vitro by the generation of NY-ESO-1 specific $CD8^+$ T-cells and $CD4^+$ T-cells.

- In addition, tumor responses will be monitored, although this is not an objective of the trial.